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IMPROVEMENTS IN POWDER COMPACTION AND ENROBING

FIELD OF THE INVENTION

This invention concerns the compacting of powder e.g. a powder containing a medicament, vitamin, dietary supplement etc, and such compacted powder being enrobed by a biodegradable and/or water soluble film, for example a non-gelatin film, such as hydroxypropyl methyl cellulose (HPMC), to produce encapsulated bodies of compacted powder, suitable for dosage forms, e.g. for human ingestion. The invention is applicable to all related dosage forms, including tablets, but for simplicity all such forms will be generally referred herein as capsules.

BACKGROUND TO THE INVENTION

Tablets are a common type of dosage form and various means for improving their properties have been tried. Current methods for coating tablets, such as pharmaceutical tablets include the using of acelacoaters or pan coaters, which spray low molecular weight HPMC grades onto tablets so imparting a surface layer, which is uniform and smooth, but opaque and low gloss. It is possible for the tablets to have embossed lettering on them. This method of coating

tablets is however time consuming and requires a high level of expertise to produce satisfactory results. Production complications such as tablet twinning are common, where two tablets become attached to one another during the spray coating operation. In addition to these problems it is necessary to compact the tablets under relatively high pressures so that they do not disintegrate during the coating process. This high level of compaction can have an adverse effect on the disintegration and dissolution rates of active ingredients contained within the capsule, for example, leading to a delay in the release of a drug to a patient, whilst the tablet slowly dissolves in the stomach of the patient.

An alternative to spray or pan coating is to use two-piece hard capsules. These are produced by a dipping process, typically a HPMC solution is used, producing half shells which interlock and thus produce an enclosed capsule. These capsules are typically opaque but glossy, and cannot have any form of embossment, as this would interfere with the overlap interlocking process. The nature of the capsule dictates that there will always be an airspace above the powder fill level. Additionally, it is not possible to compact the powder into these tablets, and this so limits the quantity of powder which can be encapsulated. It follows that this lack of

compaction can effectively reduce the amount of e.g. medicament which can be encapsulated. The existence of the air space in the capsule and lack of compaction of the powder contained within the capsule leads to a capsule that is inevitably larger than necessary.

It has also been found that, after manufacture and/or sale of two-piece hard capsules, the capsules can be easily and illegally interfered with, as it is possible to separate the two halves of the capsule and tamper with its contents and replace the two halves back together without there being any obvious change in the capsule's external appearance such to suggest to the user that there was anything wrong with the capsule. This means that it can be difficult to detect capsules which have had their contents tampered with. HPMC and certain other non-gelatin materials are suitable for ingestion by humans, so delivery capsules with gelatin walls find potential use as ingestible capsules, e.g. for the delivery of accurately metered doses of pharmaceutical preparations and dietary supplements, as a possible replacement for gelatin based capsules. Conventional tablets have already been enrobed. See for example WO 02/098394.

SUMMARY OF THE INVENTION

An aspect of the invention provides an apparatus for forming a compacted powder slug coated with a film, comprising a platen

having a pocket for receiving a vacuum formed film into the pocket and receiving a powder; and a mechanical means comprising a compression piston for compacting the powder in the pocket, the compression piston having a front face with a concave recess and a square edge around the circumference of the front face.

In an embodiment the pocket has a base formed by a lower piston, the lower piston having a front face with a concave recess and a square edge around the circumference of the front face. The front face of the lower piston further comprises at least two apertures to allow a vacuum to be formed in the pocket for vacuum forming the film. The platen further comprises an aperture to allow a vacuum to be formed between the platen and the film. An array of apertures are formed in the platen around the circumference of the pocket. The platen further comprises a recessed surface defining a raised edge forming the circumference of the pocket. The diametric clearance between the compression piston and the pocket is a fraction of the film thickness. The diametric clearance between the compression piston and the pocket is at most 35 micrometres. The diametric clearance between the lower piston and the pocket is a fraction of the film thickness. The diametric clearance between the lower piston and the pocket is at most 25 micrometres. The platen further comprises an array

of pockets. A means for preconditioning the film for temporarily retaining and heating, the means for preconditioning comprising a heated plate having a surface with an array of apertures for forming a vacuum between the heated plate and the film may be provided in the apparatus. The apparatus may further comprise a gasket for receiving and retaining the compacted powder slug to transport and release the compacted powder slug to a desired location. The gasket may comprise an aperture with a receiving side for receiving the compacted powder slug and an exit side, the receiving side having a greater diameter than the exit side.

Another aspect of the invention provides an apparatus for forming a compacted powder slug coated with a film, comprising a film preconditioner for temporarily retaining and heating the film, said film preconditioner comprising a heated plate having a surface with an array of apertures for forming a vacuum between the heated plate and the film, a platen having a pocket for receiving said preconditioned film into the pocket under vacuum, and receiving the powder; and a mechanical means for compacting the powder in said pocket.

Another aspect of the invention provides an apparatus for forming a compacted powder slug coated with a film comprising a platen comprising an array of pockets for receiving a vacuum formed film into the pockets, said pockets receiving the

powder, the platen comprising at least one aperture proximate to said pockets to allow a vacuum to be formed between the platen and the film; and a mechanical means for compacting the powder in said pocket. In an embodiment of the invention an array of apertures are formed in the platen around the circumference of the pocket.

An aspect of the invention provides an apparatus for forming a compacted powder slug coated with a film comprising a platen comprising an array of pockets for receiving a vacuum formed film into the pockets receiving the powder, the platen having a recessed surface between a plurality of raised edge profiles each forming a circumference of a pocket; mechanical means for compacting the powder in said pocket; and a cutting sleeve moveable to interfere with said raised edge profile to cut a film supported thereon.

In an embodiment, the apparatus may further comprise a turntable for holding the platen and transferring the platen during processing. The turntable may comprise four platens. The apparatus may further comprise a vacuum for cleaning the platen.

Another aspect of the invention provides an apparatus of any one of the preceding claims further comprising a dosator and a dosing unit for dosing the pocket with powder, the dosator

comprising a powder hopper for holding the powder, and a dosing head having dosing tubes for retaining powder from the powder hopper and transferring the powder to the pocket. The dosing head may have tamping pins within the tubes for pre-compacting the powder in the dosing tubes and transferring the powder from the tubes into the pocket. In an embodiment the apparatus may have a dosing unit having the mechanical means for compacting, and a dosing sledge for receiving the powder from the dosing tubes of the dosing head and dosing the pockets with the powder, the sledge moveable from a charging position to a dosing position.

Another aspect of the invention provides an apparatus for forming a compacted powder slug encapsulated with a film comprising a platen having a pocket for receiving a first vacuum formed film into the pocket and receiving a powder; a dosing means for placing the powder in a position suitable for compaction of the powder in the pocket having the first vacuum formed film with powder; a compacting mechanical means for compacting the powder; a turntable for holding the platen and rotatable to transfer the platen from one station to another station during processing, a station for applying the film into the pocket of the platen and compacting the powder to partially enrobe the compacted powder, another station for applying a second vacuum formed film onto the partially

enrobed compacted powder to completely coat the slug with film.

In an embodiment the dosing means places the powder proximate the pocket in a position suitable for compaction of the powder in the pocket having the first vacuum formed film with powder. The dosing means may dose the pockets having the first vacuum formed film with the powder.

In an embodiment the apparatus may compare a vacuum for cleaning the platen, and another station for cleaning the platen. The number of platens in the turntable may correspond to the number of stations in the apparatus. The turntable may comprise four platens for processing in another embodiment. The apparatus during said compaction may process comprise a means for isolating the compaction pressure forces from the turntable assembly.

Another aspect of the invention provides an apparatus for forming a compacted powder slug coated with a film, comprising a platen having a pocket for receiving a vacuum formed film into the pocket and receiving a powder a mechanical means for comprssing the powder in the pocket; and a gasket for receiving and retaining the comapcted powder slug to transport and release the compacted powder slug to a desired location. The gasket may comprise an aperature having a receiving side

for receiving the compacted powder slug and an exit side, the receiving side having a greater diameter the exit side. The gasket may comprise an array of apertures for receiving more than one compacted powder slug.

One aspect of the invention concerns a novel method for compacting and enrobing a powder to produce capsules with enhanced properties.

A non gelatin film layer is thermoformed tablet shaped pocket under the influence of heat and/or vacuum, and/or pressure. A pre-determined mass of powder is dosed into the film formed pocket, and compressed into a tablet shape e.g. with the aid of a piston or pistons. A partially enrobed `soft' tablet results from this process, which is then fully enrobed by a second sequence of events which involves the raising of the tablet above a platen which allows the remainder of the compressed tablet to be enrobed by a second film. Suitable tablet shaped pockets can be created by using e.g. a pair of pistons slideable within a cylinder, such pistons also having the advantage of being able to form pinch points between the platen and the top of cylinders which are useful for cutting away unwanted excess film from the (partially) enrobed tablets.

One of the aims of the present invention is to produce tamper evident capsules.

Another aim of the present invention is to produce powder filled capsules whereby the powder is enrobed with a material which may or may not form a `skin tight wrap'.

Another aim of the present invention is to produce a capsule with a high gloss surface which is able to adopt an underlying embossment, e.g. to identify a pharmaceutical tablet.

Another aim of the present invention is to produce capsules which have a flange which is almost non-discernable.

Another aim of the present invention is to enable the production of dosage forms in a wide variety of shapes and sizes, which , because of the nature of the processes involved and the properties of the product produced, includes shapes and sizes of dosage forms which have not been previously possible to make or practical to use.

Another aim of the present invention is to produce capsules with favourable properties and which contain powder or other flowable solid material which is at a favourable state of compaction and/or composition, and/or the encapsulating

medium of the capsule being fast dissolving or dissolvable (with control) pharmaceutical grade films plasticised with pharmaceutical grade materials.

Another aim of the present invention is to produce capsules, which by their nature, are easy to swallow, and more easily can be conveyed to the site where it is desirable where the active ingredients are most advantageously released.

Another aspect the present invention is a method of powder compaction to produce powder compacted slugs, which , for example can be enrobed to produce capsules which possess enhanced disintegration and dissolution properties over and above traditional tablets.

Another aspect of the present invention is a method of producing a capsule, which, at the very least can perform the same function as a conventional coated tablet, but in which the conventional tablet pressing and coating stages are replaced by a single powder enrobing process.

Another aspect of the present invention is a method of producing a capsule by enrobing powder, in which, because of the nature of capsule produced, certain ancillary ingredients necessary in conventional tablet production, can be omitted. For example, ingredients in a tablet which are added to give

structural integrity can be omitted, because the active ingredients are in powder form, relatively loosely compacted are encapsulated within a film, such film which now securely packages the powder/ingredients, thus giving integrity and forming a discrete effective dosage form. Because of the aforementioned, components contained within a tablet which are designed to disperse and break up the tablet when it has reached the site of delivery, can be omitted, as the active ingredients in the capsule according to the present invention are in a non-compacted or at least less compacted form as compared to a conventional tablet, and this lesser compaction leads to the easy release and dispersal of active ingredients once the capsule film has dissolved, e.g. at the intended site of delivery.

Another aspect of the invention provides a method of enrobing compacted powder, comprising vacuum forming a film into a pocket compacting a powder in said pocket, resulting in a partially enrobed powder slug in a pocket. Vacuum forming a second film over this powder slug to completely enrobe the powder slug, forms a discrete compacted powder filled capsule, suitable for use as a dosage form.

In yet another aspect of the present invention provides a method of enrobing compacted powder using film or films, to

form a compacted powder filled capsule, wherein the film or films forming the wall of the compacted powder filled capsule used overlap each other.

In a further aspect of the present invention provides a method of forming and/or enrobing a compacted slug wherein the level of compaction of the compacted powder is less than that necessary to reach the industry standard for the discrete slug of compacted powder to be described as a tablet.

In practising the method of the invention, the films are caused to deform to conform with the external surface of the pocket and the compacted powder slug, the films effectively forming a secure capsule, by being wrapped around the powder slug. Vacuum chamber or vacuum bed apparatus, in which the films and powder are located in a suitably shaped support and exposed to conditions of vacuum (or substantially reduced pressure) can be modified and used for this purpose. Such apparatus may be based on commercially available vacuum chamber or vacuum bed apparatus, suitably modified. Vacuum forming techniques result in the compacted powder being completely enclosed and encapsulated within a film, leading to a capsule containing compacted powder, such capsule

having enhanced and controllable properties over dosage forms currently available, such as conventional tablets.

The powders to be compacted are typically subjected to pressures between, but not limited to, 5-15 mega pascals. Examples of powders compacted and enrobed include paracetamol, ibuprofen, sorbital and multivitamin. Other powder fills which are contemplated are antacid, anti-inflammatory, anti-histamine antibiotic and anti-cholesterol drugs.

The film should be a material which is suitable for human consumption and that has sufficient flexibility and plasticity to be vacuum formable. Some film materials have suitable properties in their natural condition, but commonly it will be necessary to pre-treat the film material so that it is vacuum formable. For example, it may be necessary to expose the film material to a solvent therefor; for instance certain grades of polyvinyl alcohol (PVA) will vacuum form after application of a small amount of water to the surface thereof or when exposed to conditions of high humidity. A further generally preferred possibility, is to use a film of thermoplastic material (i.e. material capable of deforming on heating) with the film to be in heat-softened condition prior to being thermoformed by exposure to vacuum. Suitable

thermoplastic materials include modified cellulose materials, particularly hydroxypropyl methyl cellulose (HPMC) and hydroxypropyl cellulose (HPC), polyvinyl alcohol (PVA), polyethylene oxide (PEO), pectin, alginate, starches, and modified starches, and also protein films such as soya and whey protein films. The currently preferred film material is HPMC. Suitable film materials are currently available.

When using thermoplastic film, the film is typically heated prior to application to pocket or compacted powder slug, so that the film is in a heat softened deformable condition. This can be achieved by exposing the film to a source of heat e.g. an infrared heater, infrared lamps, a heated plate a hot air source etc. In the process described, a range of temperatures may be used, but by way of example only, where films of different thickness may be utilized far the first and second films in the process, a first film forming temperature of around 150 degrees centigrade may be used and for the second film forming stage, a range of approximately 70-80 degrees centigrade may be used.

During the enrobing process, films may be caused to overlap, preferably a minimum of 1.5mm-2mm. Compacted powder slugs may preferably have a sidewall height of about 3mm and films may be caused to overlap substantially completely over the sidewall area.

The film material may include optional colourings, e.g. in the form of food dyes such as FD and C yellow number 5, and/or optional flavourings, e.g. sweeteners, and/or optional textures etc in known manner.

The film material typically includes plasticiser to give desired properties of flexibility to the film in known manner. Materials used as plasticisers include alpha hydroxy as lactic acid and salts thereof, maleic acid, benzyl alcohol, certain lactones, diacetin, triacetin, propylene glycol, glycerin or mixtures thereof. A typical thermoplastic film formulation is HPMC 77% by weight, plasticiser 23% by weight.

The film suitably has a thickness in the range 20-200 microns, conveniently 50 to 100 microns, e.g. at about 80 microns, with appropriate film thickness depending on factors including the size and form of the tablet. Films of different thickness may be used, e.g. a film of greater thickness may be used in the first stage of the enrobing process, say 125 microns thickness and a film of lesser thickness may be used in the second stage of the enrobing process, say 80 microns thickness.

Because of the nature of the film forming process according to the present invention, under certain circumstances, e.g.

where the powder to be compacted contains particles which, under compaction, have the ability to pierce film, it may be advantageous to have the thickness of the film formed in the pocket to be greater than that of the film which is to cover the remainder of the compacted powder slug (in the second and final phase of enrobement of the compacted powder). Such differential thickness may give rise to certain advantageous structural features of the resultant capsule; the capsule my be generally more robust and so may be more safely stored and handled (generally thicker film on the capsule), but such capsule also possessing a smaller area (window) of weaker, thinner film which can give rise to quicker release characteristics by the thinner film wall dissolving more quickly when exposed to any given solvent. An advantageous differential film thickness to form a capsule with wall of different thickness, could be e.g. 70/90 micron film coordination to produce capsules which are robust but which release their contents quickly, through a window of thinner film.

Therefore films of different thickness may be used in the enrobing process, and to give a further examples, a film of greater thickness may be used in the first stage of the enrobing process, a maximum of 200 microns and a minimum of 70 microns but say preferably 125 microns thickness and a

film of lesser thickness may be used in the second stage of the enrobing process, a maximum of 125 microns and a minimum of 50 microns, but say preferably 80 microns thickness.

When making multiples of enrobed compacted powder slugs, the spacing of the compacted powder slugs can be important. If the compacted powder slugs are positioned too closely together, the film is not able to fully thermoform between them. For example, a spacing between the adjacent compacted powder slugs of about 4mm has been found to give good results, the film being able to fully adopt the vertical sidewall of the compacted powder slug to a distance of about 2mm before it begins to curve away from the side of the compacted powder slug.

According to one aspect of the invention, the method involves forming two separate overlapping half coatings of film, effectively on the compacted powder slug. The method preferably involves, first forming a film in a pocket, then compacting a powder slug into the film lined pocket, thereby effectively coating/encapsulating a substantial portion of a powder slug within a film formed into a partial capsule, removing the remaining film material not coating the compacted powder slug e.g. by cutting, then coating half of the compacted powder slug, with overlapping portions of the two coatings sealed together to provide a sealed complete

enclosure for the slug, and again removing remaining surplus film material not coated on the slug. It may be necessary to apply adhesive material between the overlapping film coatings e.g. to the surface of the film layers, to ensure the formation of an effective seal therebetween and to make the resultant capsule tamper-evident. The adhesive material conveniently has the same composition as the film, but with a greater proportion of plasticiser, e.g. 93% to 98% by weight plasticiser, so as to provide a less viscous material. The adhesive material may be applied, e.g. by use of a roller, spraying etc. A typical adhesive formulation, with % representing % by weight, is HPMC 4%, lactic acid 77%, water 19%.

The compacted powder slug and capsule conveniently include a generally cylindrical side wall portion, with two half coatings overlapping on this side wall. Tablets of circular symmetrical form with a circular cylindrical side wall are very common, but other forms e.g. generally oblong and oval, again including a generally cylindrical side wall, are also known.

It may be also advantageous or desirable to apply adhesive material e.g. as described above, to the surface of compacted powder slug prior to the final stage of coating, to promote

adhesion of the second portion of the film thereto. Again, this may be achieved by e.g. use of a roller, spraying etc.

A plurality of tablets in an array may be conveniently coated simultaneously, using a suitably large sheet of film material.

BRIEF DESCRIPTION OF THE DRAWINGS

Embodiments of this invention are now further described in detail, by way of example only, with reference to the drawings in which:

FIG. 1 shows in steps a-l the basic compaction and enrobing apparatus and process in accordance with an embodiment of the invention;

FIG. 2 shows a variation of the method shown in FIG.1 with steps a1 and b1 in accordance with an embodiment of the invention.

FIG. 3 shows a variation of the method shown in FIG.1 with steps a2 - d2 in accordance with an embodiment of the invention;

FIG.4 shows a variation of the method shown in FIG. 1 with steps a3 - g3 in accordance with an embodiment of the invention;

FIG.5 A-B shows a top view (filmside) and bottom view, respectively of a platen assembly in accordance with an embodiment of the invention;

FIG.6 A-B FIG.6A shows a cross-sectional view of the platen assembly of FIG. 5A taken along the arrow shown in FIG.5A in accordance with an embodiment of the invention and FIG.6B shows the section indicated by dashed circle in FIG.6A in more detail;

FIG.7 A-F show a lower piston in accordance with an embodiment of the invention, where FIG.7A and B show perspective views of the lower piston, FIG.7C shows plain view of a front face of the lower piston, FIG.7D and E show cross-sectional views of the piston taken along Y-Y and X-X as shown in FIG.7C, and FIG.7F shows the section indicated by dashed circle in FIG.7B in more detail of the concave shape in front face of piston and square edges;

FIG.8A-B FIG.8A shows a perspective view of a lower platen in accordance with an embodiment of the invention, and FIG.8B shows the section indicated by dashed circle in FIG.8A in more detail of the recessed surface around the cavities and raised edge around

cavities, also the vacuum holes around the cavities;

FIG.9A-B FIG.9A shows a cross sectional view of the lower platen of FIG.8A in accordance with an embodiment of the invention, and FIG.9B shows the section indicated by dashed circle in FIG.9A of the raised edges around the cavities;

FIG.10 shows a perspective view of the dosing unit in accordance with an embodiment of the invention;

FIG.11 shows a perspective view of the dosing unit of FIG.10 slideably engaged with base plate in accordance with an embodiment of the invention;

FIG.12 shows a front perspective view of a dosator engaged with the dosing unit of FIG.11 in accordance with an embodiment of the invention;

FIG.13 A-B FIG. 13A shows a perspective view of a shaft with vanes of dosator of FIG.12 in accordance with an embodiment of the invention, and FIG.13B shows a cross-sectional view of the shaft with vanes of FIG.13A;

FIG.14A-B shows a rear perspective view of the dosator dosing, and compaction units of FIG.12 with

compaction pistons in accordance with an embodiment of the invention, and FIG.14B shows a cross-sectional view of the dosator, dosing and compaction units of FIG.14A taken along X-X of FIG.14A;

FIG.15 A-C FIG.15 A-B show perspective views of a compaction piston in accordance with an embodiment of the invention, and FIG.15C shows the section indicated by dashed circle in FIG.15A;

FIG.16 A-B FIG.16A shows a perspective view of the dosator, dosing and compaction units of FIG.14A with pistons compressed in accordance with an embodiment of the invention; and FIG. 16B shows a cross-sectioned view of the dosator, dosing and compaction units of FIG.16A taken along X-X of FIG.16A;

FIG.17 A-B FIG.17A shows a perspective view of a thermoformer in accordance with an embodiment of the invention, and FIG.17B shows a perspective view of the underside of the assembled unit of the thermoformer of FIG.17A;

FIG.18 shows a timing diagram of a system in accordance with an embodiment of the invention;

FIG.19A-C, FIG 19A shows a perspective view of a dosator in accordance with an embodiment of the invention, FIG.19B shows the dosator powder bowl shown in FIG.19A in more detail and FIG.19C shows the dosator head shown in FIG.19A in more detail;

FIG.20A-C, FIG 20A shows a perspective view of a dosing unit and rotor head assembly in accordance with an embodiment of the invention, FIG.20B shows a dosing unit shown in FIG.20A in more detail, and FIG.20C shows the dosator dosing head shown in FIG.19C charging the dosing unit shown in FIG.20B;

FIG.21 shows a perspective view of an inkjet assembly in accordance with an embodiment of the invention;

FIG.22 shows a perspective view of a vacuum for cleaning the platen and the pockets in accordance with an embodiment of the invention;

FIG.23 shows a perspective view of a turntable for holding the platen to transfer the platen from one processing station to another processing station in accordance with an embodiment of the invention;

FIG.24 shows a perspective view of a cam unit for raising and lowering the platen from the turntable in accordance with an embodiment of the invention; and

FIG.25A-E FIG.25A shows a tablet gasket in accordance with an embodiment of the invention, FIG.25B shows a cross-sectional view taken along A-A of the gasket in FIG.25A, FIG.25C shows a cross-sectional view of the gasket positioned in a transfer arm with tablets and FIG.25D-E show cross-sectional views of the platen assembly and the gasket.

DETAILED DESCRIPTION

The drawings show the various stages of a powder compaction/enrobing process.

FIG.1 shows the mechanism of the basic steps of powder compaction and enrobement via steps a-l:

a. A first film (1) is laid upon a platen (2). Lower piston (3), slideable in cylinder (4) incorporates vacuum port (5).

b. Film (1) completely drawn down into cylinder (4) by a vacuum created by vacuum port (5) and said film (1) also resting on the crown of lower piston (3), to form a pocket shape.